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ABSTRACT

Reporting long-term ophthalmologic sequelae among ex-prematures at 6 to 10 years of age, this study compares 42 ex-premature infants who had had regressed forms of retinopathy of prematurity (ROP) during the neonatal period with 42 matched non-ROP ex-premature controls at 6 to 10 years of age. Subjects were subdivided into four groups: (1) ROP plus ophthalmologic disorders in later life; (2) ROP without ophthalmologic disorders in later life; (3) non-ROP wtih opthalmologic disorders in later life; and (4) non-ROP without ophthalmologic disorders in later life. The overall incidence of ophthalmologic problems was 55 percent in the ROP group and 36 percent in the non-ROP group. Strabismus, amblyopia and refraction anomalies occurred more frequently in the ROP group. In the ROP group, a significantly greater number of children had decreased vision in one or both eyes, compared to the non-ROP group. Although the incidence of ophthalmologic problems in the ROP group was considerably higher, the incidence in the non-ROP group still turned out unexpectedly high. This implies that non-ROP very low birth weight neonates should also be considered to be at a greatly increased risk for later visual problems. Regular ocular examinations, mandatory for the ROP group, thus should be inluded in follow-up programs of non-ROP very low birthweight neonates as well. (RH)

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Prematures with and without regressed retinopathy of prematurity: Comparison of long-term (6-10 years) ophthalmological morbidity.

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Abstract

Fourty-two ex-prematures having had regressed forms of retinopathy of prematurity (ROP) during the neonatal period were compared with 42 matched non-ROP ex-premature controls at ages 6-10 years.

The over-all incidence of ophthalmologic problems was 55% in the ROP and 36% in the non-ROP group. Strabismus, amblyopia and refraction anomalies occurred more frequently in the ROP group; in this group a significantly greater number of children had decreased vision in one or both eyes compared to the non-ROP group.

Although the incidence of ophthalmologic problems in the ROP group was considerably higher, the incidence in the non-ROP group still turned out unexpectedly high. This implicates that non-ROP very low birth weight neonates should also be considered to be at a greatly increased risk for later visual problems. Regular ocular examinations, mandatory for the ROP group, thus should be included in follow-up programs of non-ROP very low birthweight neonates as well!

Prematures surviving the neonatal period are commonly supposed to have an increased risk for developing ophthalmological problems.[1 2 3] Myopia, strabismus (squint), amblyopia, delayed visual maturation and blindness are encountered more frequently in premature than in term born cohorts.[4] A number of studies have related ocular sequelae to neonatal retinopathy of prematurity (ROP).[5 6] However, it has as well been suggested that prematurity per se could influence postnatal ocular development in such a way to increase later ophthalmologic abnormalities.[7 8]

Most follow-up studies published hitherto cover fairly short periods of one to three years.[1 2 3 5 6] It has been suggested[6] that apparently adequate vision in infants could contribute to the loss of patients in follow-up and a lack of understanding of subsequent ocular morbidity.

The purpose of this study is to report long-term ophthalmologic sequelae (at ages 6-10 years) amongst ex-prematures. We were able to document these in 84 out of 112 children previously included in a 4 year survey of ROP.[9] Half of the children had ROP during the neonatal period (either regressing spontaneously or after cryotherapy), the other half had been matched controls without ROP.

Subjects and methods

Patients included in this study were born and admitted to the neonatal intensive care unit (NICU) of the Wilhelmina Children's Hospital from 1 April 1977 to 31 March 1981.

From the 53 ROP cases and 56 non-ROP controls originally described,[9] the ophthalmologic status of 42 children from each group was documented throughout 1987 i.e. at ages 6-10 years. Parents initially completed a questionnaire inquiring about the general condition, schoolperformance and ophthalmologic problems of their children. All parents of children not seen at our own follow-up clinic permitted their ophthalmologists to be approached for detailed information about their past and present ophthalmologic status.

We did not exclude children with sequelae probably relating to the neonatal period (i.e. with neurologic, developmental, behavioural abnormality). No children needed to be excluded because of the familiar occurrence of strabismus, high myopia and/or astigmatism.

Ophthalmologic investigations consisted of inspection and cover tests (for squint), visual acuity assessment (by means of test-symbols; pictures and E-hooks) followed by the instillation of 0,5% cyclopentolate drops with ten minute intervals; refraction was measured by streak retinoscopy 30-40 minutes later.
We documented constant and intermittent heterotropia (manifest squint), amblyopia, negative refractive values (myopia) and positive refractive values (hypermetropia) of ≥ 1 diopter (D) and astigmatism.

Until 1983 ROP was graded in our hospital according to the Patz modification[10] of Reese's classification.[11] With the aid of the original description and still available fundus drawings, patients were reclassified according to the international classification of retinopathy of prematurity (ICROP).[12]

General results

Children were subdivided into four groups:

a. ROP + ophthalmologic disorders in later life (n = 23)

b. ROP without ophthalmologic disorders in later life (n = 19)

c. non-ROP + ophthalmologic disorders in later life (n = 15)

d. non-ROP without ophthalmologic disorders in later life (n = 27)

The incidence of later ophthalmologic disorders in the ROP group (55%) was considerably higher than in the non-ROP group (36%) ($p = 0,08$).

General characteristics from the neonatal period are represented in table 1. From this table it appears that children with later visual problems had the longest (group a) as well as the shortest (group c) mean duration of supplementary oxygen administration. Thus, oxygen does not seem to relate to later visual problems except when resulting in ROP.

Disabilities possibly related to the neonatal period are represented in table 2. Distinct differences between the four groups cannot be demonstrated.

Ophthalmological results

Pertinent data were obtained from all 23 ROP and 14 of 15 non-ROP childrens with later ophthalmological abnormalities (strabismus, amblyopia, anisometropia). No precise data could be obtained of one non-ROP child whose parents mentioned visual problems, because his ophthalmologist had emigrated and access to his files was impossible.

Ophthalmologic data are represented in table 3. From this table it is apparent that 23 out of 42 (55%) of the ROP children and 15 out of 42 (36%) of non-ROP children (have) had ophthalmological problems on follow-up.

In the neonatal period three children had stage III^{+} disease. They underwent cryotherapy of the avascular retina; on follow-up two have subnormal vision of both eyes, one has substantially decreased vision of both eyes and attends a school for visually handicapped children. Two children had late retinal detachment (at ages 1½ and 9 years) and cryotherapy. One had stage 1, the other stage 2 ROP during the neonatal period. The relation between neonatal ROP-grade and later visual problems is represented in table 4. A considerable difference is found between children with stage 3 and children with stages 1 and 2. Six out of seven stage 3 children have subsequent problems vs seventeen out of thirty-five stage 1 and 2 children ($p = 0.07$). The difference between stage 3 ROP and non-ROP children is significant ($p < 0.05$).

Discussion

Prematurity and very low birthweight are increasingly mentioned as risk factors for ocular morbidity. Keith and Kitchen[1] concluded that in premature babies without cerebral palsy and free from ROP, squint or astigmatism occurs in approximately 18%. Curtin[4] found myopia in 20.6% of 34 prematures; Graham and Grey[13] noted myopia in 33% of 150 prematures. The myopia of prematurity is known to regress during the first years of life with emergence of emmetropic/ hyperopic refractions later on.[4]

A number of studies on NICU-populations do not allow an estimation of the over-all incidence of ocular problems in later life because follow-up is too short. The main objective of this study was to document ophthalmological problems in children with regressed forms of ROP in comparison with children without ROP in the neonatal period, after a 6-10 years follow-up period.

We found the incidence of strabismus with or without amblyopia to be remarkably high in both groups. The strabismus incidence of 25% over-all (30% in the ROP, 20% in the non-ROP group) and the amblyopia incidence of 12% over-all (21.5% in the ROP, 2.5% in the non-ROP group) considerably exceed incidences mentioned in schoolchildren; however, they well agree with incidence reports in other premature cohorts (table 5).

Myopia and astigmatism were present in 29% of ROP and in 10% of non-ROP children. The incidence of myopia in the ROP group is in agreement with reports from other authors,[2] [15] usually describing cohorts at much younger ages. Although the myopia prevalence in premature populations is higher than in term-born cohorts (table 5), the myopia tends to regress during the first year of life, resulting in emmetropic and/or hyperopic refractions. This shift towards normalization does not seem to occur in ROP-eyes, which may result in a permanent myopia, often of high degree.

Decreased vision (in at least one eye) is a very prominent feature in the ROP group. Our data do not elucidate whether decreased vision should be attributed to retinal abnormalities or amblyopia or both. All together the risk for diminished vision seems to be one of the consequences of ROP even when it apparently healed completely.

We conclude that the incidence of 55% ocular problems makes regular ophthalmologic examinations in the ROP group mandatory. The 36% incidence in the non-ROP group implies that follow-up in these children should thoroughly survey their ophthalmologic status as well.

Both groups show a high incidence of strabismus. The concomittant amblyopia risk is evident in the ROP group. Accessory risks for the ROP-group are higher degrees of myopia (which may be associated with poor school performance), and eye threatening pathology such as late retinal ablative disease.

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Legends to tables:

Table 1: Neonatal characteristics of ROP and non-ROP children; group a and c with, b and d without later ophthalmologic problems

Table 2: Sequelae probably relating to the neonatal period (a, b, c, d: see text under general results)

Table 3: Ophthalmologic data of ROP and non-ROP children at ages 6-10 years

Table 4: Relation of neonatal ROP-grade with later ophthalmological problems (see table 3)

Table 5: Myopia, amblyopia and strabismus prevalence in childhood

table 1

	ROP		non-ROP	
	group a	group b	group c	group d
n	23	19	15	27
mean birthweight (gr); range	1075 (760-1720)	1160 (750-1710)	1135 (510-1480)	1145 (760-1870)
mean gestational age (wk); range	29.2 (24-35)	28.2 (25-32)	28.9 (27-31)	29 (26-34)
♀ : ♂	13 : 10	10 : 9	6 : 9	11 : 16
artificial ventilation (n)	13	9	6	14
O2 > 40% (n)	19	17	14	25
duration suppl. O2 (days); range	19.4 (0-65)	14.5 (0-45)	8 (0-50)	12.1 (0-49)

table 2

	group a	group b	group c	group d
school for visually handicapped	1	-	-	-
hearing deficit	-	1	-	1
developmental delay	4	2	3	1
motor disturbance	3	2	1	-
behavioural abnormality	-	-	1	2
cerebral palsy	2	-	1	-
consistent growth retardation	-	-	-	1

table 3

	ROP	non-ROP	
n	42	42	
no ophthalmological problems (n)	19	27	N.S.* (p = 0,08)
with ophthalmological problems (n)	23	15	
I strabismus	13	8	N.S.*
amblyopia	9	1	
strabismus + amblyopia	6	1	
strabismus - amblyopia	7	7	
amblyopia - strabismus	3	-	
II refraction anomalies			
myopia 1 - 3 D	5	3	N.S.* (p = 0,06)
myopia > 3 D	7	1	
astigmatism ≤ 2 D	7	2	N.S.* (p = 0,06)
astigmatism > 2 D	5	2	
hypermetropism 1 - 3 D	4	3	
hypermetropism > 3 D	1	1	
unknown	-	1	
III decreased vision	13	2	p < 0,05*
subnormal one eye (0,3-0,7)	6	2	
subnormal both eyes	4	-	
substantial decrease, one eye (0,12-0,28)	2	-	
substantial decrease, both eyes	1	-	
unknown	-	1	

* Fisher's exact 2 x 2t with Yates correction

N.S. = not significant

table 4

	ophthalmological problems	
	+	-
non-ROP	15	27
grade 1	7	9
grade 2	10	9
grade 3	6	1

table 5

	Author(s)	n	subjects	age (yrs)	prevalence	
MYOPIA	Alward 1985[14]	252	young adults	?	6.8%	< -0.5 D
	Fledelius 1976[15]	523	schoolchildren	9-11	9.3%	all negative refractive values
	Gerhard e.a. 1978[16]	60	all prematures <1500 g 1200-1500 g <1200 g	5-8	30% 28% 72%	not stated
	Nissenkorn e.a. 1983[2]	155	prematures (600-2000 g) - 42 prematures with ROP - 113 prematures without ROP	2-8	25% 50% 15.9%	< -0.25 D
	Keith & Kitchen 1983[1]	111	prematures (500-1500 g) - 11 prematures with ROP - all refractive errors	2	55% 17%	< -2 D
	This study	84	prematures (510-1870 g) - 42 ROP - 42 non-ROP	6-10	19.3% 29% 10%	≤ -1 D
AMBLYOPIA	McNail 1955[17]	12568	schoolchildren	5-19	1.3%	
	Bangerter 1955[18]	3300	schoolchildren	4-18	2.8%	
	Van Beek 1964[19]	18449	schoolchildren	4-19	2.5%	
	This study	84	prematures (510-1870 g) - 42 ROP - 42 non-ROP	6-10	12% 21.5% 2.4%	
STRABISMUS	McNail 1955[17]	12568	schoolchildren	5-19	2.7%	manifest squint
	Van Beek 1964[19]	18449	schoolchildren	4-19	3.6%	manifest and latent squint
	Keith & Kitchen 1983[1]	111	prematures (500-1500 g)	2	19%	manifest squint
	This study	84	prematures (510-1870 g) - 42 ROP - 42 non-ROP	6-10	25% 31% 19%	manifest and intermittent squint